PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 12530000/PDB/MLO	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/AU2004/001536	International filing date *(day/month/year)* 5 November 2004	Priority date *(day/month/year)* 5 November 2003
International Patent Classification (IPC) or national classification and IPC Int. Cl. [7] A61K 9/10		
Applicant THE AUSTRALIAN NATIONAL UNIVERSITY *et al.*		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. [X] *(sent to the applicant and to the International Bureau)* a total of 2 sheets, as follows:
      - [ ] sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      - [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

[X]	Box No. I	Basis of the report
[ ]	Box No. II	Priority
[ ]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[ ]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[ ]	Box No. VI	Certain documents cited
[ ]	Box No. VII	Certain defects in the international application
[ ]	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of the report
1 September 2005	27 October 2005 8 NOV 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer NORMAN BLOM Telephone No. (02) 6283 2238

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Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1 (b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

☐ the international application as originally filed/furnished

☒ the description:

pages **1-27** as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☒ the claims:

pages **28** as originally filed/furnished
pages* as amended (together with any statement) under Article 19
pages* **29-30** received by this Authority on **1 September 2005** with the letter of 1 September 2005
pages* received by this Authority on with the letter of

☐ the drawings:

pages as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims **1-27**	**YES**
	Claims **none**	**NO**
Inventive step (IS)	Claims **1-27**	**YES**
	Claims **none**	**NO**
Industrial applicability (IA)	Claims **1-27**	**YES**
	Claims **none**	**NO**

2. Citations and explanations (Rule 70.7)

New Citation

Patent Abstracts of Japan **JP 2001-178362** (Toi Shigeo) 3 July 2001

The following documents cited in the International Search Report (ISR) have been considered for the purposes of this report:

- D1: WO 1999/039696
- D2: Chem. Pharm. Bull. (2003), 51 (2), 171-174,
- D3: European Journal of Pharmaceutical Sciences (2002), 16, 37-43,
- D4: J. Pharm. Pharmac., (1977), 29, 163-168,
- D5: J. Pharm. Pharmacol., (1991), 43, 317-324,
- D6: Art. Cells, Blood Subs., and Immob. Biotech., (1994), 22 (4), 1007-1018,
- D7: Journal of Pharmaceutical Sciences (1975), 64 (5), 793-797,
- D8: Journal of Pharmaceutical sciences (1998), 87 (4), 514-518,
- D9: Journal of Pharmaceutical Sciences (1975), 64 (9), 1475-1481,
- D10: Pharmaceutical Research (2004), 21 (2), 245-253.

Novelty (N) and Inventive Step (IS): Claims 1-27

The claims are considered to be novel and inventive in the light of any one or combination of two or more of document D1 to D10, referred to above, because none of these documents disclose a method for preparing a dispersion of a hydrophobic pharmaceutically active agent in an aqueous phase by combining the pharmaceutically active agent and the aqueous phase and before, during or after said combining removing dissolved gases from one or both the active agent and the aqueous phase.

The closes prior art is considered to be **JP 2001-178362** which discloses a method for producing homogenous mixed liquid of an aqueous liquid with an oily liquid without using an emulsifier (see paragraph [0004] of the computer generated English translation). The method comprises filling a flexible container with an aqueous liquid and an oily liquid. The oily liquid may contain dissolved oil soluble matter (see paragraph [0006] of the computer generated English translation).

(continued)

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box No. V 2. Citations and explanations

The container is degassed/deaerated and sealed and then exposed to a pressure of ≥6000 kg/cm^2 for 10 minutes in a liquid medium. This process is capable of sterilization of the inside of the flexible container, an essential prerequisite for parenteral pharmaceutical compositions. This method may be used for the manufacture of food (such as a food dressing), cosmetics (such as a milky lotion), perfume and other uses (see paragraphs [0003], [0007] and [0011] of the computer generated English translation). The example discloses the preparation of a homogenous mixture of an edible oil and water, free of emulsifiers and which is stable for at least 12 hours. Although the description does not elaborate on the technique used to deacrate/degas the flexible container and its contents prior to sealing, it would appear that degassed/deaerate involves merely removing any gas from above the mixture of oil and water such that the sealed bag does not contain any gas pockets.

10. The method according to claim 1 or 2 wherein at least 80-99.99% of dissolved gases are removed.

11. A dispersion of a hydrophobic pharmaceutically active agent in an aqueous phase, substantially free of dissolved gases.

12. A dispersion of droplets of a liquid or oily hydrophobic pharmaceutically active agent, or a hydrophobic pharmaceutically active agent dissolved or dispersed in a carrier oil or liquid, in an aqueous phase, wherein the droplets have an interfacial tension of about 15-55 mJm^{-2}.

13. A drug delivery system comprising a dispersion of a hydrophobic pharmaceutically active agent in an aqueous phase, substantially free of dissolved gases.

14. A drug delivery system comprising a dispersion of a hydrophobic pharmaceutically active agent in an aqueous phase, substantially free of stabilizers, surfactants and dispersants.

15. A drug delivery system comprising a dispersion of droplets of a liquid or oily hydrophobic pharmaceutically active agent, or a hydrophobic pharmaceutically active agent dissolved or dispersed in a carrier oil or liquid, in an aqueous phase wherein the droplets have an interfacial tension of about 15-55 mJm^{-2}.

16. The dispersion according to claim 12 or the drug delivery system according to claim 15 wherein the droplets have an interfacial tension of about 30-50 mJm^{-2}.

17. The dispersion according to any one of claims 11-12 or the drug delivery system according to any one of claims 13-15 wherein said agent is a finely divided solid.

18. The dispersion according to any one of claims 11-12 or the drug delivery system according to any one of claims 13-15 wherein said agent is an oil or liquid.

19. The dispersion or drug delivery system according to claim 18 wherein the agent is a perfluorocarbon.

20. The dispersion according to any one of claims 11-12 or the drug delivery system according to any one of claims 13-15 wherein the agent is dissolved or dispersed in a pharmaceutically acceptable hydrophobic carrier oil or liquid.

21. The dispersion or drug delivery system according to claim 20 wherein the carrier oil or liquid is soybean oil or a perfluorocarbon.

22. A drug delivery system according to any one of claims 13, 14 or 15 for injection.

23. A drug delivery system according to any one of claims 13, 14 or 15 for inhalation.

24. A method of delivering a hydrophobic pharmaceutically active agent to a patient in need thereof comprising administering to said patient a drug delivery system according to any one of claims 13, 14 or 15.

25. The method according to claim 24 wherein the drug delivery system is administered via injection.

26. The method according to claim 24 wherein the drug delivery system is administered via an aerosol.

27. A method for preparing a dispersion of a hydrophobic pharmaceutically active agent comprising the step of removing dissolved gases from a mixture of said agent and aqeuous phase; and, optionally, agitating or shaking the degassed mixture.